REMARKS

Claims 1, 3-7, 13, 17, 18, 20, 23-28, and 30-32 have been canceled without prejudice. Applicant reserves the right to pursue the subject matter of the canceled claims in a related application. Claim 14 has been amended to remove a limitation "or rat" and to clarify that embryonic stem cells and blastocysts are "mouse" origin. No new matter has been introduced by this amendment. The following addresses the substance of the Office Action.

Compliance with 35 USC §112

The Examiner has maintained rejections of Claims 8, 14, 15, 22, 33, 34, 37 and 38 under 35 U.S.C. §112, first paragraph as allegedly lacking enablement. More specifically, the Examiner believes that even though the human parkin2 shares a high percentage of sequence similarity with the mouse homologue, whether the mouse Parkin2 comprising the same mutation as the human would produce the same Parkinson's symptoms is unpredictable because the genetic control elements and genetic backgrounds of human and rodent are very different. The Examiner has invited the Applicant to provide recent references that teach that the phenotype of one transgenic specie is predictable of the same phenotype of another specie (i.e. from human to mouse). The Applicant had provided such references in the response to the Office Action of November 20, 2003. During the personal interview with the Examiner, conducted on June 28, 2004, the Examiner indicated that submission of data in the form of a Declaration under 37 C.F.R. §1.132 would be helpful in resolving the enablement issues raised by the Examiner. The Applicant submitted such a Declaration on August 23, 2004. In this document, the Inventor, Dr. Lubbert, provided data which shows an example of a transgenic mouse obtained by the claimed method. This transgenic mouse has a mutant mouse parkin2 gene with a deletion of the exon 3, and it indeed exhibits behavioral impairments. This exemplary parkin2 mutant transgenic mice have reduced homecage activity, show deficit in habituation to a novel environmental contexts, have abnormality of dopaminergic system, and they also showed altered anxiety-related behavior in 2 separate tests (light-dark exploration and Morris water maze). Therefore, the transgenic parkin2 mouse as claimed is useful in investigating the role of parkin2 gene disruption on various types of animal behavior.

The Examiner in the present Office Action has maintained that "production of transgenic mouse with a specific phenotype is unpredictable because of essential genetic control elements

and genetic background varies from species to species". However, the presently claimed invention is not related to any specific phenotype. Rather, the invention relates to a method of making a transgenic mouse and a transgenic mouse having specific recited mutations in the mouse *parkin2* gene. The recited mutations are in a gene from the same species as the host. Since the essential genetic control elements and essential genetic background are for the same species, there is a reasonably predictable outcome from the genetic disruption of the gene. Specifically a less active or inactive mouse parkin2 protein is expressed (see, Specification 5:8-15).

The Specification lists numerous specific mutations of the mouse parkin2 gene in Tables 1 and 2. To a person with an ordinary skill in the art, from the description of the mutations in Table 1 it is apparent that the result of the listed mutations is expression of abnormal parkin2 protein or no expression of it at all. Table 2 lists additional point mutations in mouse parkin2 gene the outcome of which is expression of an abnormal mouse parkin2 protein. How to make these listed mutations by homologous recombination is well-known in the art (see Specification 4:9-30). How to introduce these mutations into mouse embryonic stem cells is also routine as well as how to make a mouse that carries the mutated gene (see Specification, 19:7-20:19). While these procedures may be tedious, they do not constitute "undue experimentation." In fact, the inventor has produced an example of the transgenic mouse as claimed using the claimed method. Therefore, Claims 8, 14, 15, 22, 33, 34, 37 and 38 are enabled. Furthermore, in this produced transgenic mouse disruption of the parkin2 gene by introducing a deletion in Exon 3 caused expression of a protein which is only ¼ of the length of the wild-type parkin2 protein (wild-type: 461 aa, SEQ ID NO: 4, mutant: 105 aa, SEQ ID NO: 21). As predicted, the fist tests performed with the mouse showed abnormalities. Therefore, a skilled person will view the provided data as reasonably predictive of the asserted utility of the mouse of the present invention for testing the role of parkin2 protein in behavior.

Therefore, the transgenic mouse as claimed in independent Claim 8 and the claimed method of the currently amended independent Claim 14, as well as claims 15, 22, 33, 34, 37 and 38 which depend on Claims 8 or 14 are enabled and have utility.

The Examiner has rejected Claims 14, 22, 34 and 38 under 35 USC §112, second paragraph as being indefinite. More specifically, the independent Claim 14 was found indefinite

for reciting "or rat" in the last line and for not specifying that the embryonic stem cells are mouse embryonic stem cells. Applicant has amended Claim 14 accordingly. Therefore, Claims 14, 22, 34 and 38 are now definite and their rejection under 35 USC §112, second paragraph should be withdrawn.

CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Final Office Action and as discussed during personal interview on June 28, 2004. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. In light of the above amendments, remarks, and the Inventor's Declaration submitted herewith, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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